

ORIGINAL RESEARCH ARTICLE

Effects of probiotic therapy combined with personalized nursing on immune function and nursing compliance in children with acute gastroenteritis

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Abstract

This was an original study that mainly explored the effect of probiotic therapy and personalized nursing on immune function in children with acute gastroenteritis. One hundred and twelve (112) children with acute gastroenteritis were selected and divided into an intervention group and a control group. The control group accepted omeprazole enteric-coated capsules and routine nursing. In addition to omeprazole enteric-coated capsules, the intervention group additionally received probiotic therapy. The results showed that in comparison with the control group, the intervention group presented shorter time for relieving fever, vomiting, abdominal pain and diarrhea, lower levels of inflammatory factors, better improvements of immune function. The intervention group also showed higher rate of nursing compliance and nursing satisfaction. We conclude that probiotic therapy combined with personalized nursing can reduce inflammatory response, improve immune function and promote nursing compliance in children with acute gastroenteritis. (*Afr J Reprod Health* 2024; 28 [11]: 96-104)

Keywords: Acute gastroenteritis, probiotic, personalized nursing, inflammatory response, immune function, nursing compliance.

Résumé

Il s'agissait d'une étude originale qui explorait principalement l'effet de la thérapie probiotique et des soins infirmiers personnalisés sur la fonction immunitaire chez les enfants atteints de gastro-entérite aiguë. Cent douze (112) enfants atteints de gastro-entérite aiguë ont été sélectionnés et répartis en un groupe d'intervention et un groupe témoin. Le groupe témoin a accepté les capsules entérosolubles d'oméprazole et les soins infirmiers de routine. En plus des capsules entérosolubles d'oméprazole, le groupe d'intervention a également reçu un traitement probiotique. Les résultats ont montré que par rapport au groupe témoin, le groupe d'intervention présentait un temps plus court pour soulager la fièvre, les vomissements, les douleurs abdominales et la diarrhée, des niveaux plus faibles de facteurs inflammatoires et de meilleures améliorations de la fonction immunitaire. Le groupe d'intervention a également montré un taux plus élevé de conformité et de satisfaction des soins infirmiers. Nous concluons qu'une thérapie probiotique combinée à des soins infirmiers personnalisés peut réduire la réponse inflammatoire, améliorer la fonction immunitaire et favoriser l'observance des soins infirmiers chez les enfants atteints de gastro-entérite aiguë. (*Afr J Reprod Health* 2024; 28 [11]: 96-104).

Mots-clés: Gastro-entérite aiguë, probiotique, soins infirmiers personnalisés, réponse inflammatoire, fonction immunitaire, observance infirmière

Introduction

Acute gastroenteritis is a kind of digestive tract disease caused by multi-pathogens and multi-factors, and is more common in children¹. This is due to the fact that the immune system and function of the gastrointestinal tract of infants and young children are not mature, their resistance to external infections is poor, and they cannot adapt to large changes in food.² Acute gastroenteritis in children occurs frequently in summer and autumn, and the

clinical symptoms are mainly presented as diarrhea, loss of appetite, fever, and vomiting³. In severe cases, there may be dehydration, poisoning symptoms, irritability, lethargy, and even coma, which will not only bring great pain to infants and young children, but also seriously affect their health⁴.

The clinical treatment of acute gastroenteritis includes symptomatic treatment and etiological treatment⁵. Omeprazole is a proton pump inhibitor, which suppresses the secretion of gastric parietal

cells and gastric acid, so as to change the gastric environment and protect the gastric mucosa⁶. Over the past few decades, studies have reported the utilization of probiotics in treating acute gastroenteritis, especially in children⁷. Probiotics are a general term for a large class of living microorganisms, including *Lactobacillus* and *bifidobacterium*, which are beneficial to human intestinal and even whole-body health⁸. These microorganisms can prevent the growth of pathogenic bacteria in the intestine, and promote intestinal digestion as well as the absorption and metabolism of special nutrients⁹. Its mechanism of action is to competitively antagonize harmful bacteria, secrete metabolites with antibacterial activity, conserve intestinal mucosal epithelium, and regulate systemic immunity¹⁰.

In addition, children with acute gastroenteritis are younger in age, often cry and do not cooperate in the treatment process. Their compliance rate is poor, which will not only impact on the emotions of children's families and the doctor-patient relationship, but also affect the smooth progress of treatment¹¹. Therefore, the clinical consensus is that it is essential to combine symptomatic treatment with effective nursing interventions. Personalized nursing is a common nursing model in clinical nursing in recent years, it can develop personalized nursing plans according to the different needs and situations of patients, and fully reflect the people-oriented nursing concept of "understanding people, respecting people, caring for people"¹². The objective of this study was to explore the impacts of probiotic therapy plus personalized nursing on immune function and nursing compliance in children with acute gastroenteritis. The novelty of our study is that probiotic therapy combined with personalized nursing can reduce inflammatory response, improve immune function and promote nursing compliance in children with acute gastroenteritis, which provide clinical reference for the treatment and nursing for children with acute gastroenteritis.

Methods

Materials

One hundred and twelve children with acute gastroenteritis accepted therapy in The First Hospital

of China Medical University from January 2022 to December 2023 were selected and they were divided into an intervention group and control group utilizing the dynamic randomization method. Each group had 56 children. The control group had 30 boys and 26 girls, aged 3-8 years old, with an average age of (5.50±1.55) years. The onset time was 2-15 days, with an average age of (8.50±2.12) days. The intervention group had 28 boys and 28 girls, aged 2-9 years old, with an average age of (5.56±1.58) years. The onset time was 3-14 days, with an average age of (8.43±2.10) days. No difference was seen in general data between 2 groups ($P>0.05$).

Diagnostic criteria were as described in previous literature⁴. Inclusion criteria included the following: (1) children diagnosed with acute gastroenteritis; and (2) child's family accepting to participate in the study and signed the consent form. The exclusion criteria were children with: (1) comorbidity with malignant tumour disease; (2) severe circulatory diseases and systemic infections; (3) liver and kidney insufficiency; (4) immune system deficiency; (5) those allergic to the drugs; (5) cognitive impairment of their guardians; and (6) incomplete data.

Treatment methods

After admission, patients in two groups received symptomatic treatment measures such as correcting water and electrolyte disorder, rehydration, and cooling. The control group accepted omeprazole enteric-coated capsules (Guangdong P. D. Pharmaceutical Co., Ltd.), 20 mg/time, 1-2 times/day, lasted for 14 days.

In addition to omeprazole enteric-coated capsules, the intervention group additionally received probiotic therapy, called Combined *Bifidobacterium*, *Lactobacillus*, *Enterococcus* and *Bacillus cereus* Tablets, Live (Hangzhou Yuanda Bio-pharmaceutical Co., LTD., specification: 0.5 g/piece) with warm water after meals, 3 tablets/times, 3 times/day, lasted for 14 days.

Nursing methods

The control group accepted routine nursing. The nursing staff provided medication guidance for the

children, ensured that the mothers of the children followed the doctor's advice on time and in accordance with the amount of medication, and formulated a reasonable dietary plan for the children, ensured body nutrition, and replenished water for the children in time.

In contrast, the intervention group received personalized nursing. Other procedures carried out for this group included the following;

Personalized health education. For children with poor understanding ability, the nursing staff developed disease publicity brochures in the form of cartoons, and explained disease knowledge to children in the form of video animation.

Personalized medication care. The nursing staff explained in detail the importance of complying with medical drugs for the family of the child, made a medication list according to the needs and diet of the child, told the child to take medication on time following the list, and customized a medication alarm clock to remind the child to take medicine on time. This also includes the family giving certain rewards to encourage the child to take the medications.

Personalized condition care. The nursing staff inspected the ward every once in a while, actively communicated with the children, observed the changes in the expression of the children during this period, kept the children in a static state by playing games, measured their temperature to prevent the deterioration of the disease, and promptly informed the doctor once abnormalities were found.

Personalized environmental care. The nursing staff kept the ward environment clean, reasonably controlled the temperature and humidity in the ward, put green plants or posters in safe places, placed cartoon characters and dolls of interest to children, and regularly disinfected and ventilated them.

Personalized diet care. The nursing staff made a personalized diet plan according to the children's condition and combined with the children's dietary preferences.

During the period, children were inquired whether they were satisfied with the diet plan, if they were not satisfied, timely adjustment was made, and the family members of the younger ones gave opinions or suggestions.

Observed outcome indicators

The following outcome indicators were measured in both control and intervention groups:

(1) *Time for relief of clinical symptoms.* Time for relief of clinical symptoms including fever, vomiting, abdominal pain, and diarrhea were recorded in 2 groups.

(2) *Levels of inflammatory factors.* Three ml of fasting venous blood was obtained from the children with venipuncture, and serum was taken after 3000 r/min centrifugation for 10 min. The levels of inflammatory markers consisting of interleukin-6 (IL-6), procalcitonin (PCT), and hypersensitive C-reactive protein (hs-CRP) were measured with enzyme-linked immunosorbent assay (ELISA).

(3) *Immune function.* Three ml fasting venous blood was obtained from the children, and sera were taken after 3000 r/min centrifugation for 10 min. The levels of serum CD4⁺ and CD8⁺ were analyzed by flow cytometry, followed by calculation of CD4⁺/CD8⁺.

(4) *Incidence of adverse reactions.* The total incidence of adverse reactions including dizziness, flatulence, erythema and hyperpyrexia was recorded in the two groups. (5) *Nursing compliance.* The compliance of children was evaluated based on the degree of treatment cooperation such as dressing change, medication, examination, etc. Complete compliance included: The child did not struggle or cry during care, took medication on time, and was willing to receive treatment. Partial compliance: During the nursing process, the child had mild panic, no struggle, crying, emotional stability after comfort, and was willing to accept treatment and take medication. Non-compliance: The child had poor cooperation in the process of nursing, crying, struggling, emotional instability after reassurance, and refused to accept treatment and medication. Compliance rate = (number of complete compliance + number of partial compliance)/total compliance × 100%. (6) *Nursing satisfaction.* The nursing satisfaction questionnaire was distributed to the family members before discharge, ranging 0-100 points. Among them, 75-100 points were satisfied, 50-74 points were basically satisfied, and <50 points were dissatisfied.

Nursing satisfaction = (number of satisfied cases + number of basically satisfied cases)/total number of cases $\times 100\%$.

Statistical analysis

SPSS 24.0 statistical software was implemented for data analysis. Measurement data were exhibited as ($\bar{x} \pm s$), followed by t-test for comparison. Count data were exhibited as (n, %), followed by χ^2 test for comparison. $P < 0.05$ meant statistical significance.

Ethical considerations

Our study was approved by the Ethical Committee of The First Hospital of China Medical University in December 2021.

Results

Time for relieving clinical symptoms in 2 groups

In contrast to the control group, the time for relieving fever, vomiting, abdominal pain and diarrhea in the intervention group was shorter ($P < 0.01$, Figure 1).

Levels of inflammatory factors in the two groups

Prior to intervention, no differences were discovered in levels of inflammatory factors between the two groups ($P > 0.05$). After intervention, hs-CRP, PCT along with IL-6 levels declined in two groups. When compared with the control group, the inflammatory factors in the intervention group were lower ($P < 0.01$, Figure 2).

Immune function in the two groups

Prior to intervention, no differences were discovered in indicators of immune function between the two groups ($P > 0.05$). After intervention, $CD4^+$ and $CD4^+/CD8^+$ levels were elevated while $CD8^+$ level was declined in the two groups. The improvements of the above immune function indicators in the intervention group were significantly greater as compared to the control group ($P < 0.01$, Figure 3).

Incidence of adverse reactions in 2 group

Table 1 shows that there no difference in the incidence of adverse reactions between the two groups ($P > 0.05$).

Nursing compliance in 2 groups

As compared to the control group, the intervention group presented better nursing compliance rate ($P < 0.05$, Table 2).

Nursing satisfaction in 2 groups

In comparison with the control group, the intervention group presented better nursing satisfaction ($P < 0.05$, Table 3).

Discussion

Acute gastroenteritis belongs to a common disorder in children's gastrointestinal tract¹³. In comparison with adults, children are more susceptible to disease because of their weak defense against pathogenic bacteria¹⁴. Nausea, vomiting, fever, and diarrhea are common symptoms of the disease. Prolonged diarrhea and vomiting may easily lead to dehydration¹⁵. If not treated in time, intestinal bleeding, intestinal perforation, and other complications may be caused, posing a great threat to children's quality of life and life safety¹⁶.

Omeprazole belongs to a group of drugs for treating digestive system diseases, which can block the production of gastric acid, improve the gastrointestinal environment, and protect the gastric mucosa¹⁷. Nevertheless, reports have pointed out that the therapeutic effect of this drug is not apparent when given to children, and further improvement is needed.

Probiotics are active microorganisms that are beneficial to the human body, which are able to accelerate gastrointestinal peristalsis, accelerate the digestion and absorption of nutrients, enhance the body's antioxidant level, inhibit gastrointestinal inflammation, etc., and are suitable for people possessing low immunity and diarrhea¹⁸.

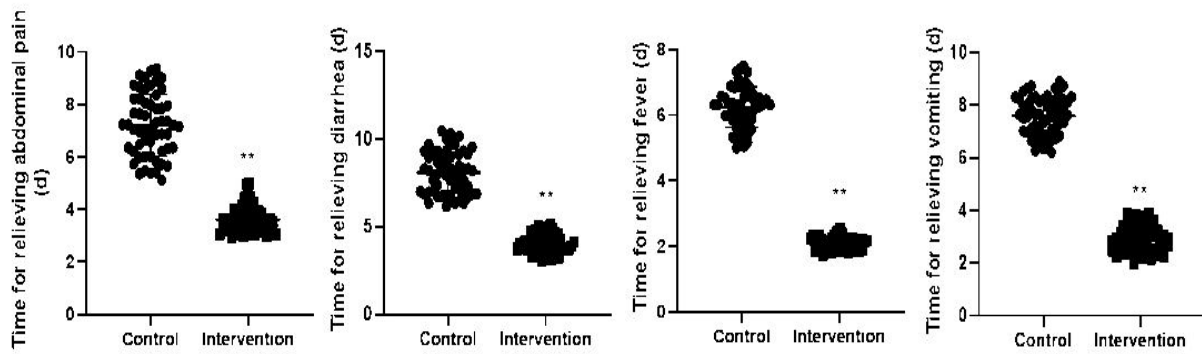


Figure 1: Time for relieving clinical symptoms in 2 groups. **P<0.01

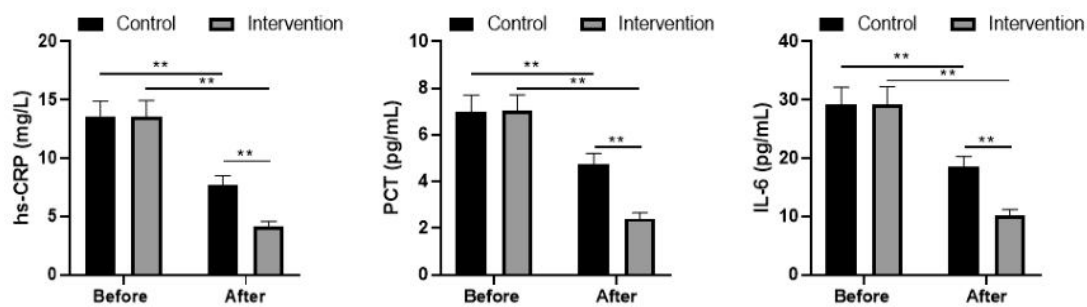


Figure 2: Levels of inflammatory factors in the two groups. **P<0.01

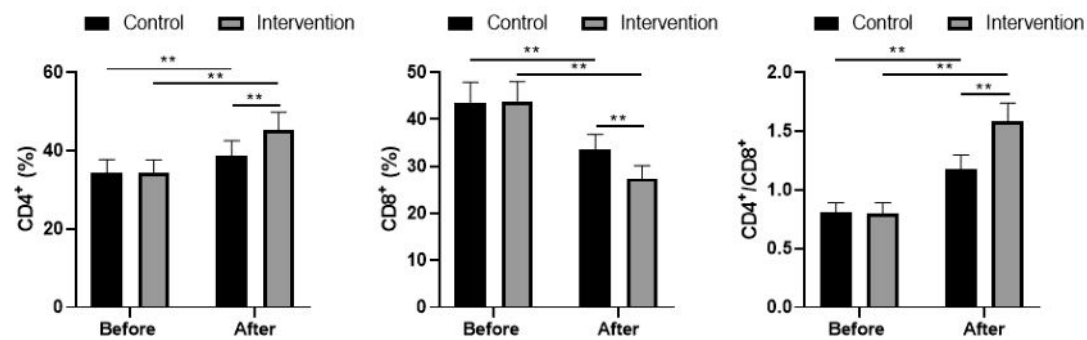


Figure 3: Immune function in two groups. **P<0.01.

Table 1: Incidence of adverse reactions in 2 groups

Groups	N	Dizziness	Flatulence	Erythema	Hyperpyrexia	Total incidence rate
Control group	56	2 (3.57)	1 (1.79)	2 (3.57)	0	5 (8.93)
Intervention group	56	1 (1.79)	1 (1.79)	1 (1.79)	0	3 (5.37)
χ^2						0.538
P						0.463

Table 2: Nursing compliance in 2 groups

Groups	N	Complete compliance	Partial compliance	Non-compliance	Total compliance rate
Control group	56	13 (23.21)	32 (57.14)	11 (19.65)	45 (80.35)
Intervention group	56	20 (35.71)	33 (58.93)	3 (5.36)	53 (94.64)
χ^2					5.224
P					0.022

Table 3: Nursing satisfaction in 2 groups

Groups	N	Satisfied	Basically satisfied	Dissatisfied	Total satisfaction rate
Control group	56	20 (35.71)	26 (46.43)	10 (17.86)	46 (82.14)
Intervention group	56	25 (44.64)	29 (51.79)	2 (3.57)	54 (96.43)
χ^2					5.973
P					0.014

Studies have manifested that probiotics have a crucial role in the management of pediatric gastrointestinal disorders, acute gastroenteritis included¹⁹. In clinical treatment, pediatric patients are a more special group. Children are younger, their bodies are not fully developed, their resistance and immunity are poor, and they are vulnerable to bacteria²⁰. Similarly, children's language of expression and communication skills are poor, and they cannot accurately express their own needs in the treatment process²¹. The nurses in the routine nursing mode cannot fully understand the condition of children, and cannot give correct help to children, which affects the recovery speed of children's disease²². Consequently, nursing staff should offer more high-quality nursing mode for children, comprehensively understand the needs of children, and improve the treatment compliance of children, which will greatly improve the prognosis of children.

Personalized nursing belongs to a nursing model that has emerged over the past few years, which refers to that nursing staff implement comprehensive, personalized and intimate care for patients. This begins from the perspectives of patients, understanding their thoughts, and formulating nursing specific methods to address patients' current physical conditions²³. The application of personalized nursing model has narrowed the relationship between nurses and patients, and improved the status of nurses in the hearts of patients²⁴. According to the relevant data,

the implementation of personalized nursing model can effectively relieve the adverse emotions of children, improve clinical symptoms along with improve nursing quality and nursing satisfaction²⁵.

In our study, the results suggested that in contrast to the control group, the time for relieving fever, vomiting, abdominal pain and diarrhea in the intervention group was shorter, and the nursing compliance rate and nursing satisfaction were higher. This suggests that probiotic therapy combined with personalized nursing could improve the clinical symptoms, promote the compliance and nursing satisfaction of children with acute gastroenteritis. Tetralogy of viable bifidobacterium tablets contain beneficial bacteria such as bifidobacterium and *Enterococcus faecalis*, which helps to change the intestinal flora, inhibiting some pathogenic bacteria in the intestine, maintaining the normal intestinal peristalsis, regulating the balance of intestinal flora, and ultimately contributing to the improvement of clinical manifestations²⁶.

Available studies suggest that, inflammation and infection run through the entire process of acute gastroenteritis in children, which will break the balance of immune function along with aggravate the acute inflammatory response of the body and gastrointestinal mucosa²⁷. Hs-CRP is a typical inflammatory index reflecting the inflammatory response in the body, and it possesses high sensitivity in diagnosing the degree of inflammatory response in children. In the initial stage of inflammation²⁸, IL-6 is a crucial inflammatory

effector cell implicated in the pathological mechanism of the body's inflammatory response, and with the intensification of the body's inflammatory response, this index shows an increasing trend²⁹. As one of the important indicators to assess the systemic inflammatory response in children, PCT has good stability. Once the inflammatory response occurs in the body, PCT is highly expressed³⁰. The results of our study suggest that by comparing the control group, hs-CRP, PCT along with IL-6 levels in the intervention group were lower after intervention, reflecting that probiotic therapy plus personalized nursing could reduce the inflammatory response in children with acute gastroenteritis. This may be attributable to the tetralogy of viable bifidobacterium tablet that can not only directly supplement the normal flora in the body of children, but also inhibit some pathogenic bacteria, promote gastrointestinal motility in children, quickly establish intestinal flora homeostasis, restore the normal intestinal defense mechanism, and diminish the level of inflammatory markers in the body of children³¹.

Moreover, our study manifested that after intervention, CD4⁺ and CD4⁺/CD8⁺ levels were elevated whereas CD8⁺ level declined in the two groups. The improvements of these immune function indexes in the intervention group were more significant as compared with the control group, implying that probiotic therapy plus personalized nursing could promote the immune function of children with acute gastroenteritis. Tetralogy of viable bifidobacterium tablet can supplement the missing intestinal flora in children's intestines, promote the functional recovery of intestinal mucosa, improve the defense function of intestinal mucosa against pathogenic bacteria, maintain the balance of intestinal flora, relieve the symptoms of diarrhea in children, promote the proliferation of immune cells, and further improve the immune function of children³².

Limitations of the study

Strengths of the study were that it was a randomized clinical trial that included multiple measures related to inflammation and immune function. Our study indicated that probiotic therapy combined with

personalized nursing can reduce inflammatory response, improve immune function and promote nursing compliance in children with acute gastroenteritis, which provide clinical reference for the treatment and nursing for children with acute gastroenteritis. Limitations were small sample and without follow-up.

Conclusion

Probiotic therapy combined with personalized nursing can reduce inflammatory response, improve immune function and promote nursing compliance in children with acute gastroenteritis.

Authors' contributions

Li SQ and Li FF: conceived and designed the study, collected and analysed the data, and prepared the manuscript. All authors mentioned in the article approved the manuscript.

Acknowledgments

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References

1. Schnadower D, Tarr PI, Casper TC, Gorelick MH, Dean JM, O'Connell KJ, Mahajan P, Levine AC, Bhatt SR, Roskind CG, Powell EC, Rogers AJ, Vance C, Sapien RE, Olsen CS, Metheny M, Dickey VP, Hall-Moore C and Freedman SB. Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children. *N Engl J Med.* 2018; 379(21):2002-2014.
2. Posovszky C, Buderus S, Classen M, Lawrenz B, Keller KM and Koletzko S. Acute Infectious Gastroenteritis in Infancy and Childhood. *Dtsch Arztebl Int.* 2020; 117(37):615-624.
3. Hartman S, Brown E, Loomis E and Russell HA. Gastroenteritis in Children. *Am Fam Physician.* 2019; 99(3):159-165.
4. Guarino A, Aguilar J, Berkley J, Broekaert I, Vazquez-Frias R, Holtz L, Lo Vecchio A, Meskini T, Moore S, Rivera Medina JF, Sandhu B, Smarrazzo A, Szajewska H and Treepongkaruna S. Acute Gastroenteritis in Children of the World: What Needs to Be Done? *J Pediatr Gastroenterol Nutr.* 2020; 70(5):694-701.
5. Freedman SB, Ali S, Oleszczuk M, Gouin S and Hartling L. Treatment of acute gastroenteritis in children: an overview of systematic reviews of interventions commonly used in developed countries. *Evidence-*

- based child health : a Cochrane review journal. 2013; 8(4):1123-37.
6. Lin X, Chen H and Lin YN. The clinical efficacy and safety of atropine combined with omeprazole in the treatment of patients with acute gastritis: a systematic review and meta-analysis. *Ann Palliat Med.* 2021; 10(9):9535-9543.
 7. Freedman SB, Finkelstein Y, Pang XL, Chui L, Tarr PI, VanBuren JM, Olsen C, Lee BE, Hall-Moore CA, Sapien R, O'Connell K, Levine AC, Poonai N, Roskind C, Schuh S, Rogers A, Bhatt S, Gouin S, Mahajan P, Vance C, Hurlley K, Powell EC, Farion KJ and Schnadower D. Pathogen-Specific Effects of Probiotics in Children With Acute Gastroenteritis Seeking Emergency Care: A Randomized Trial. *Clin Infect Dis.* 2022; 75(1):55-64.
 8. Suez J, Zmora N, Segal E and Elinav E. The pros, cons, and many unknowns of probiotics. *Nat Med.* 2019; 25(5):716-729.
 9. LaMont JT. Probiotics for Children with Gastroenteritis. *N Engl J Med.* 2018; 379(21):2076-2077.
 10. Depoorter L and Vandenplas Y. Probiotics in Pediatrics. A Review and Practical Guide. *Nutrients.* 2021; 13(7)
 11. Brondani JP and Pedro ENR. The use of children's stories in nursing care for the child: an integrative review. *Rev Bras Enferm.* 2019; 72(suppl 3):333-342.
 12. Linder LA. Contributions of Pediatric Oncology Nursing to Advance Care and Reduce Disparities Among Children and Adolescents with Cancer: Introduction. *Semin Oncol Nurs.* 2021; 37(3):151-165.
 13. Elliott EJ. Acute gastroenteritis in children. *Bmj.* 2007; 334(7583):35-40.
 14. Wielgos K, Setkowicz W, Pasternak G and Lewandowicz-Uszyńska A. [Management of acute gastroenteritis in children]. *Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego.* 2019; 47(278):76-79.
 15. Stanyevic B, Sepich M, Biondi S, Baroncelli GI, Peroni D and Di Cicco M. The evolving epidemiology of acute gastroenteritis in hospitalized children in Italy. *Eur J Pediatr.* 2022; 181(1):349-358.
 16. Polich M, Mannino-Avila E, Edmunds M, Rungvivatjarus J, Patel A, Stucky-Fisher E and Rhee KE. Disparities in Management of Acute Gastroenteritis in Hospitalized Children. *Hospital pediatrics.* 2023; 13(12):1106-1114.
 17. Richter JE, Kahrilas PJ, Johanson J, Maton P, Breiter JR, Hwang C, Marino V, Hamelin B and Levine JG. Efficacy and safety of esomeprazole compared with omeprazole in GERD patients with erosive esophagitis: a randomized controlled trial. *Am J Gastroenterol.* 2001; 96(3):656-65.
 18. Alli SR, Gorbovskaya I, Liu JCW, Kolla NJ, Brown L and Müller DJ. The Gut Microbiome in Depression and Potential Benefit of Prebiotics, Probiotics and Synbiotics: A Systematic Review of Clinical Trials and Observational Studies. *Int J Mol Sci.* 2022; 23(9)
 19. Szajewska H, Berni Canani R, Domellöf M, Guarino A, Hojsak I, Indrio F, Lo Vecchio A, Mihatsch WA, Mosca A, Orel R, Salvatore S, Shamir R, van den Akker CHP, van Goudoever JB, Vandenplas Y and Weizman Z. Probiotics for the Management of Pediatric Gastrointestinal Disorders: Position Paper of the ESPGHAN Special Interest Group on Gut Microbiota and Modifications. *J Pediatr Gastroenterol Nutr.* 2023; 76(2):232-247.
 20. Hull K and Clarke D. Restraining children for clinical procedures: a review of the issues issues that continue to challenge children's nursing. *Br J Nurs.* 2010; 19(6):346-50.
 21. Coetzee M, Leonard A, Bonaconsa C, Power N and North N. Developing children's nursing care outcome statements in Africa using World Café methods. *Int Nurs Rev.* 2020; 67(4):529-534.
 22. Wang Z, Shao Y, Yang L, Li X and Hao L. Nursing care for children with fulminant myocarditis treated with extracorporeal membrane oxygenation. *Medicine (Baltimore).* 2023; 102(44):e35682.
 23. Pazarcikci F and Efe E. Effects of Comfort-Oriented Nursing Care Based on the Comfort Theory on Perioperative Anxiety and Fear in Children Undergoing Surgical Circumcision: RCT. *J Perianesth Nurs.* 2023; 38(2):236-245.
 24. Pless IB, Feeley N, Gottlieb L, Rowat K, Dougherty G and Willard B. A randomized trial of a nursing intervention to promote the adjustment of children with chronic physical disorders. *Pediatrics.* 1994; 94(1):70-5.
 25. Vélchez Barboza V, Klijn TP, Salazar Molina A and Sáez Carrillo KL. Effectiveness of personalized face-to-face and telephone nursing counseling interventions for cardiovascular risk factors: a controlled clinical trial. *Revista latino-americana de enfermagem.* 2016; 24:e2747.
 26. Kluijfhout S, Trieu TV and Vandenplas Y. Efficacy of the Probiotic Probiological Confirmed in Acute Gastroenteritis. *Pediatric gastroenterology, hepatology & nutrition.* 2020; 23(5):464-471.
 27. Small CL, Xing L, McPhee JB, Law HT and Coombes BK. Acute Infectious Gastroenteritis Potentiates a Crohn's Disease Pathobiont to Fuel Ongoing Inflammation in the Post-Infectious Period. *PLoS pathogens.* 2016; 12(10):e1005907.
 28. Carbone F, Elia E, Casula M, Bonaventura A, Liberale L, Bertolotto M, Artom N, Minetti S, Dallegri F, Contini P, Verzola D, Pontremoli R, Viazzi F, Viviani GL, Bertolini S, Pende A, Pisciotta L and Montecucco F. Baseline hs-CRP predicts hypertension remission in metabolic syndrome. *European journal of clinical investigation.* 2019; 49(8):e13128.
 29. Soler MF, Abaurrea A, Azcoaga P, Araujo AM and Caffarel MM. New perspectives in cancer immunotherapy: targeting IL-6 cytokine family. *J Immunother Cancer.* 2023; 11(11)
 30. Simon L, Gauvin F, Amre DK, Saint-Louis P and Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review

- and meta-analysis. *Clin Infect Dis.* 2004; 39(2):206-17.
31. Freedman SB, Xie J, Nettel-Aguirre A, Pang XL, Chui L, Williamson-Urquhart S, Schnadower D, Schuh S, Sherman PM, Lee BE, Gouin S, Farion KJ, Poonai N, Hurley KF, Qiu Y, Ghandi B, Lloyd C and Finkelstein Y. A randomized trial evaluating virus-specific effects of a combination probiotic in children with acute gastroenteritis. *Nat Commun.* 2020; 11(1):2533.
32. Yang J, Kuang H, Li N, Hamdy AM and Song J. The modulation and mechanism of probiotic-derived polysaccharide capsules on the immune response in allergic diseases. *Crit Rev Food Sci Nutr.* 2023; 63(27):8768-8780